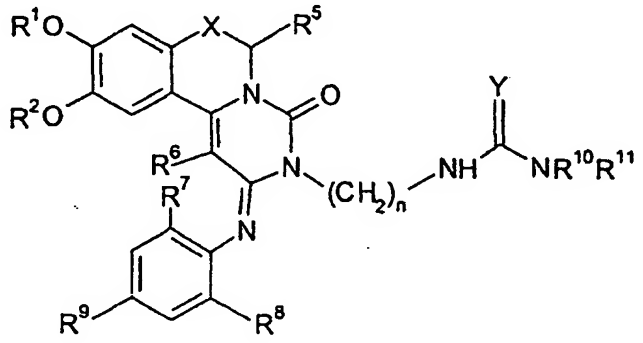
AMENDMENTS TO THE CLAIMS

Claims 1-42 (cancelled).

Claim 43 (currently amended): A method for the ~~acute or prophylactic~~ treatment of a disease in a mammal, wherein the disease is characterized by being amenable to treatment with ~~where~~ a phosphodiesterase isoenzyme inhibitor and/or a bronchodilator ~~would be expected to be of benefit~~, which method comprises administering to said mammal an effective, non-toxic amount of a compound of ~~general~~ formula I:



I

wherein

each of R^1 and R^2 independently represents a C_{1-6} alkyl or C_{2-7} acyl group;

R^5 represents a hydrogen atom or a C_{1-3} alkyl, C_{2-3} alkenyl or C_{2-3} alkynyl group;

R^6 represents a hydrogen atom or a C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, amino, C_{1-6} alkylamino, di(C_{1-6}) alkylamino or C_{2-7} acylamino group;

each of R^7 and R^8 independently represents a hydrogen or halogen atom or a hydroxy, trifluoromethyl, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-7} acyl, C_{1-6} alkylthio, C_{1-6} alkoxy,

C_{3-6} cycloalkyl; and

R^9 represents a hydrogen or halogen atom or a hydroxy, trifluoromethyl, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-7} acyl, C_{1-6} alkylthio, C_{1-6} alkoxy or C_{3-6} cycloalkyl group;

X represents a group CR^3R^4, wherein each of R^3 and R^4 independently represents a hydrogen atom or a C_{1-3} alkyl group;

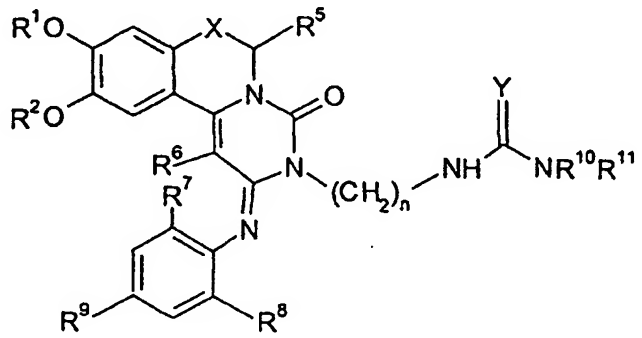
each of R^{10} and R^{11} independently represents a hydrogen atom, a C_{1-3} alkyl, C_{3-6} cycloalkyl or phenyl group;

Y represents an oxygen atom or a group $CHNO_2$, NCN, NH or NNO_2;

n is an integer from 2 to 4;

or a salt thereof.

Claim 44 (currently amended): A method for the ~~acute or prophylactic~~ treatment of asthma in a mammal, which method comprises administering to said mammal an effective, non-toxic amount of a compound of ~~general~~ formula I:



I

wherein

each of R^1 and R^2 independently represents a C_{1-6} alkyl or C_{2-7} acyl group;

R^5 represents a hydrogen atom or a C_{1-3} alkyl, C_{2-3} alkenyl or C_{2-3} alkynyl group;

R^6 represents a hydrogen atom or a C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, amino, C_{1-6} alkylamino, di(C_{1-6}) alkylamino or C_{2-7} acylamino group;

each of R^7 and R^8 independently represents a hydrogen or halogen atom or a hydroxy, trifluoromethyl, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-7} acyl, C_{1-6} alkylthio, C_{1-6} alkoxy,

C_{3-6} cycloalkyl; and

R^9 represents a hydrogen or halogen atom or a hydroxy, trifluoromethyl, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-7} acyl, C_{1-6} alkylthio, C_{1-6} alkoxy or C_{3-6} cycloalkyl group;

X represents a group CR^3R^4, wherein each of R^3 and R^4 independently represents a hydrogen atom or a C_{1-3} alkyl group;

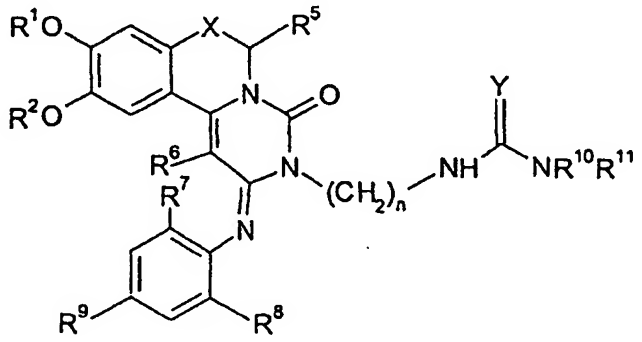
each of R^{10} and R^{11} independently represents a hydrogen atom, a C_{1-3} alkyl, C_{3-6} cycloalkyl or phenyl group;

Y represents an oxygen atom or a group $CHNO_2$, NCN, NH or NNO_2;

n is an integer from 2 to 4;

or a salt thereof.

Claim 45 (currently amended): A method for the ~~acute or prophylactic~~ treatment of chronic obstructive pulmonary disease (COPD) in a mammal, which method comprises administering to said mammal an effective, non-toxic amount of a compound of ~~general~~ formula I:



I

wherein

each of R^1 and R^2 independently represents a C_{1-6} alkyl or C_{2-7} acyl group;

R^5 represents a hydrogen atom or a C_{1-3} alkyl, C_{2-3} alkenyl or C_{2-3} alkynyl group;

R^6 represents a hydrogen atom or a C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, amino, C_{1-6} alkylamino, di(C_{1-6}) alkylamino or C_{2-7} acylamino group;

each of R^7 and R^8 independently represents a hydrogen or halogen atom or a hydroxy, trifluoromethyl, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-7} acyl, C_{1-6} alkylthio, C_{1-6} alkoxy,

C_{3-6} cycloalkyl; and

R^9 represents a hydrogen or halogen atom or a hydroxy, trifluoromethyl, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-7} acyl, C_{1-6} alkylthio, C_{1-6} alkoxy or C_{3-6} cycloalkyl group;

X represents a group CR^3R^4, wherein each of R^3 and R^4 independently represents a hydrogen atom or a C_{1-3} alkyl group;

each of R^{10} and R^{11} independently represents a hydrogen atom, a C_{1-3} alkyl, C_{3-6} cycloalkyl or phenyl group;

Y represents an oxygen atom or a group $CHNO_2$, NCN, NH or NNO_2;

n is an integer from 2 to 4;

or a salt thereof.

Claim 46 (currently amended): A method as claimed in any <u>one</u> of claims 43, 44 or 45, wherein independently or in any compatible combination:

each of R^1 and R^2 independently represent a C_{1-6} alkyl;

each of R^3 and R^4 represents a hydrogen atom;

R^5 represents a hydrogen atom;

R^6 represents a hydrogen atom;

each of R^7 and R^8 independently represent a C_{1-6} alkyl;

R^9 represents a halogen atom or a methyl or acetyl group;

Y represents an oxygen atom or a group $CHNO_2$; and

n is 2.

Claim 47 (currently amended): A method as claimed in any one of claims 43 to 45, wherein the compound is administered by aerosol.

Claim 48 (currently amended): A method as claimed in any one of claims 43 to 45, wherein the ~~animal~~ mammal is a human.

Claims 49-50 (cancelled).

Claim 51 (currently amended): A method as claimed in any one of claims 43 to 45, wherein each of R^1 and R^2 represents a C_{1-4} alkyl group; and each of R^7 and R^8 represents a methyl, ethyl or isopropyl group.

Claim 52 (currently amended): A method as claimed in any one of claims 43 to 45, wherein the compound of general formula I is selected from the group consisting of:

9,10-Dimethoxy-2-(2,4,6-trimethylphenylimino)-3-(*N*-carbamoyl-2-aminoethyl)-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-a]isoquinolin-4-one;

9,10-Dimethoxy-2-(2,4,6-trimethylphenylimino)-3-[*N*-(*N'*-isopropylcarbamoyl)-2-aminoethyl]-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-a]isoquinolin-4-one;

9,10-Dimethoxy-2-(2,4,6-trimethylphenylimino)-3-[*N*-[1-(*N'*-methyl-2-nitroethenamine)]-2-aminoethyl]-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-a]isoquinolin-4-one;

9,10-Dimethoxy-2-(2,4,6-trimethylphenylimino)-3- [N-[1-(*N'*-isopropyl-2-nitroethenamine)]-2-aminoethyl]-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-a]isoquinolin-4-one;

9,10-Dimethoxy-2-(2,4,6-trimethylphenylimino)-3-[*N*-[1-(*N'*, *N'*-dimethyl-2-nitroethenamine)]-2-aminoethyl]-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-a]isoquinolin-4-one;

9,10-Dimethoxy-2-(2,4,6-trimethylphenylimino)-3-[*N*-(*N'*-phenylcarbamoyl)-2-aminoethyl]-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-a]isoquinolin-2-one;

9, 10-Dimethoxy-3-[2-guanidinoethyl]-2-(2,4,6-trimethylphenylimino)-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-a]isoquinolin-4-one;

9,10-Dimethoxy-3-[*N*-(*N'*-nitro)-2-guanidinoethyl]-2-(2,4,6-trimethylphenylimino)-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-a]isoquinolin-4-one;

3-[*N*-(*N'*-Cyclohexylcarbamoyl)-2-aminoethyl]-9,10-dimethoxy-2-(2,4,6-trimethyl-phenylimino)-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-a]isoquinolin-4-one;

3-(*N*-Carbamoyl-2-aminoethyl)-9,10-dimethoxy-2-(2-methylphenylimino)-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-a]isoquinolin-4-one;

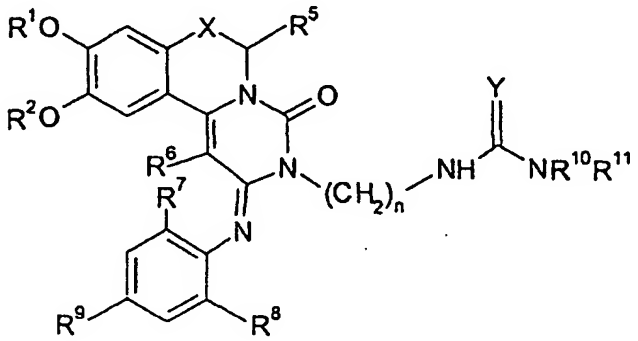
3-(*N*-Carbamoyl-2-aminoethyl)-2-(2,6-diisopropylphenylimino)-9,10-dimethoxy-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-a]isoquinolin-4-one;

3-(*N*-Carbamoyl-4-aminobutyl)-9,10-dimethoxy-2-(2,4,6-trimethylphenylimino)-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-a]isoquinolin-4-one; and

3-[*N*-(*N'*-Cyano-*N"*-methyl)-2-guanidinoethyl]-9,10-dimethoxy-2-(2,4,6-trimethyl-phenylimino)- 3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-a]isoquinolin-4-one.

Claim 53 (currently amended): A method of treating a mammal ~~suffering from or susceptible to a disease, disorder or condition mediated by PDE III and PDE IV isoenzymes~~ in need of a smooth muscle relaxant and/or an anti-inflammatory compound, comprising administering to a subject an effective, non-toxic amount of a compound of formula I:

~~formula I:~~



I

wherein

each of R^1 and R^2 independently represents a C_{1-6} alkyl or C_{2-7} acyl group;

R^5 represents a hydrogen atom or a C_{1-3} alkyl, C_{2-3} alkenyl or C_{2-3} alkynyl group;

R^6 represents a hydrogen atom or a C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, amino, C_{1-6} alkylamino, di(C_{1-6}) alkylamino or C_{2-7} acylamino group;

each of R^7 and R^8 independently represents a hydrogen or halogen atom or a hydroxy, trifluoromethyl, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-7} acyl, C_{1-6} alkylthio, C_{1-6} alkoxy,

C_{3-6} cycloalkyl; and

R^9 represents a hydrogen or halogen atom or a hydroxy, trifluoromethyl, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-7} acyl, C_{1-6} alkylthio, C_{1-6} alkoxy or C_{3-6} cycloalkyl group;

X represents a group CR^3R^4, wherein each of R^3 and R^4 independently represents a hydrogen atom or a C_{1-3} alkyl group;

each of R^{10} and R^{11} independently represents a hydrogen atom, a C_{1-3} alkyl, C_{3-6} cycloalkyl or phenyl group;

Y represents an oxygen atom or a group $CHNO_2$, NCN, NH or NNO_2;

n is an integer from 2 to 4;

or a salt thereof.

Claim 54 (currently amended): The method of claim 53, wherein the mammal suffers from ~~disease, disorder or condition mediated by PDE III and PDE IV isoenzymes is~~ a respiratory disorder, skin disorder or auto-immune disease in which increasing intracellular concentrations of cAMP is considered beneficial.

Claim 55 (previously presented): The method of claim 54, wherein the respiratory disorder is selected from the group consisting of asthma, allergic asthma, hay fever, allergic rhinitis, bronchitis, chronic obstructive pulmonary disease (COPD), adult respiratory distress syndrome (ARDS), and cystic fibrosis.

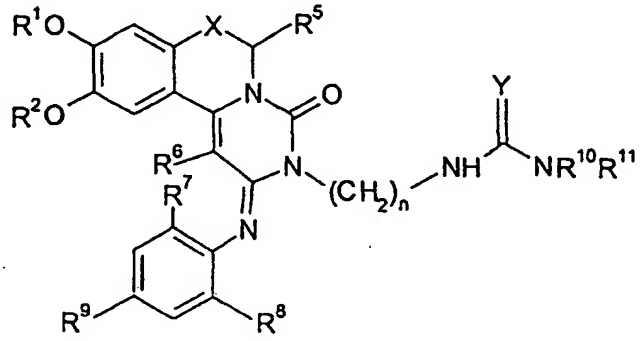
Claim 56 (previously presented): The method of claim 54, wherein the skin disorder is selected from the group consisting of atopic dermatitis and psoriasis,

Claim 57 (currently amended): The method of claim 53, wherein the mammal suffers from ~~disease, disorder or condition mediated by PDE III and PDE IV isoenzymes is characterized by~~ ocular inflammation or cerebral ischaemia.

Claim 58 (new): The method of claim 43, wherein the disease is characterized by an increased eosinophil count in lung of the mammal.

Claim 59 (new): The method of claim 43, wherein the phosphodiesterase inhibitor is a phosphodiesterase type III inhibitor or a phosphodiesterase type IV inhibitor.

Claim 60 (new): A method to treat asthma or to cause bronchial dilation in a mammal in need thereof, comprising administering to said mammal an effective, non-toxic amount of a compound of formula I:



I

wherein

each of R^1 and R^2 independently represents a C_{1-6} alkyl or C_{2-7} acyl group;

R^5 represents a hydrogen atom or a C_{1-3} alkyl, C_{2-3} alkenyl or C_{2-3} alkynyl group;

R^6 represents a hydrogen atom or a C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, amino, C_{1-6} alkylamino, di(C_{1-6}) alkylamino or C_{2-7} acylamino group;

each of R^7 and R^8 independently represents a hydrogen or halogen atom or a hydroxy, trifluoromethyl, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-7} acyl, C_{1-6} alkylthio, C_{1-6} alkoxy,

C_{3-6} cycloalkyl; and

R^9 represents a hydrogen or halogen atom or a hydroxy, trifluoromethyl, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-7} acyl, C_{1-6} alkylthio, C_{1-6} alkoxy or C_{3-6} cycloalkyl group;

X represents a group CR^3R^4, wherein each of R^3 and R^4 independently represents a hydrogen atom or a C_{1-3} alkyl group;

each of R^{10} and R^{11} independently represents a hydrogen atom, a C_{1-3} alkyl, C_{3-6} cycloalkyl or phenyl group;

Y represents an oxygen atom or a group $CHNO_2$, NCN, NH or NNO_2;

n is an integer from 2 to 4;

or a salt thereof.

Claim 61 (new): The method of claim 60, wherein independently or in any compatible combination:

each of R^1 and R^2 independently represent a C_{1-6} alkyl;

each of R^3 and R^4 represents a hydrogen atom;

R^5 represents a hydrogen atom;

R^6 represents a hydrogen atom;

each of R^7 and R^8 independently represent a C_{1-6} alkyl;

R^9 represents a halogen atom or a methyl or acetyl group;

Y represents an oxygen atom or a group $CHNO_2$; and

n is 2.

Claim 62 (new): The method of claim 60, wherein the compound is administered by aerosol.

Claim 63 (new): The method of claim 60, wherein the mammal is a human.